Reference values for quantitative analysis of Gd-contrast enhancement kinetics in skeletal muscle NMR imaging.

Decorte Nicolas[1], Laurie Cabrol[1], Mathilde Drouet[1], Noura Azzabou[1], and Pierre G. Carlier[1]
[1]*Institute of Myology, CEA, Paris, 75013, France*

Introduction: Abnormal skeletal muscle enhancement post Gd-contrast agent (Gd-CA) injection is a commonly recognized feature on NMR images in inflammatory diseases but also in chronic interstitial fibrosis or in conditions where sarcolemma permeability is increased such as in muscle dystrophy (1, 2). Yet, these data have almost always been qualitatively interpreted, and no reference values have ever been acquired in order to determine precisely the abnormality threshold of Gd enhancement. However, when it comes to monitoring lesions severity in longitudinal studies, these benchmarks become mandatory. Our aim here, was to quantify the skeletal muscle relaxivity changes after Gd-CA injection to normal subjects.

Materials and Methods: Twelve healthy volunteers, six male (age range: 22-62 yr) and six female (age range: 22-67 yr) were scanned in a 3T whole-body magnet. Imaging was centered on the thighs. A slice selective inversion-recovery TurboFlash sequence (TR 10s, TI 1.2s, flip angle 8°, TE 1.64ms, FOV 400mm, 5 slices) was run during a 3min baseline period before intravenous injection of 0.1 mmol/kg of Gd-DOTA. Acquisitions were carried on for one hour in order to follow most of the Gd-CA enhancement kinetics. For each slice, regions of interest (ROIs) were drawn on 8 muscles of both thighs and ROI signal intensities were normalized to baseline values.

Left Thigh	RF	VI	VL	VM
K^{trans} (min^{-1})	0.089 ± 0.056	0.140 ± 0.091	0.113 ± 0.057	0.148 ± 0.086
K_{ep} (min^{-1})	0.416 ± 0.301	0.622 ± 0.428	0.548 ± 0.326	0.632 ± 0.386
V_e	0.237 ± 0.060	0.243 ± 0.050	0.227 ± 0.049	0.251 ± 0.047
Right Thigh	**RF**	**VI**	**VL**	**VM**
K^{trans} (min^{-1})	0.069 ± 0.036	0.162 ± 0.106	0.130 ± 0.073	0.159 ± 0.081
K_{ep} (min^{-1})	0.357 ± 0.156	0.653 ± 0.472	0.568 ± 0.347	0.620 ± 0.368
V_e	0.206 ± 0.070	0.276 ± 0.064	0.257 ± 0.072	0.280 ± 0.059

Table 1. Description of Gd-DOTA enhancement with Tofts constants in healthy subjects (Mean ±SD).
RF: Rectus Femoris, VI, Vastus Intermedius, VL: Vastus Lateralis, VM: Vastus Medialis.

Using the Gd-DOTA relaxivity constant measured in blood at 3T,, the changes in skeletal muscle relaxivities were calculated for each individual muscle. In order to extract constants proposed by Tofts (3), we simulated the arterial input function (C_{p0}) with data from the literature and using this relation $C_t(t) = v_e.C_{p0}.e^{-K_{ep}t}$, with $k_{ep} = K^{trans} / v_e$. The concentration Gd-DOTA curve was fitted by a nonlinear fit including the arterial input function (Matlab, Mathworks Sofware,,USA).

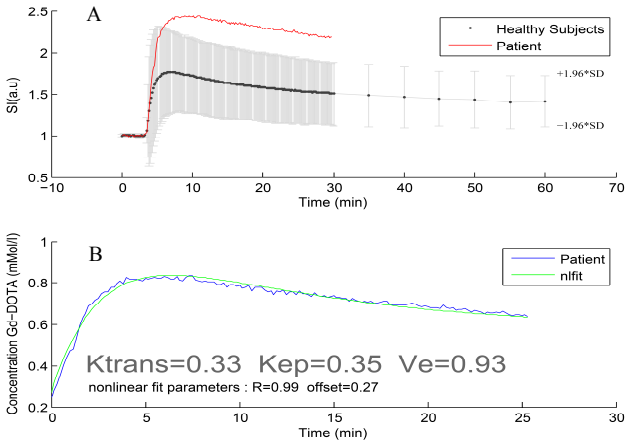

Figure 1. Illustration of typical abnormal Gd-DOTA signal intensity (SI) enhancement of Vastus lateralis in patient with inflammatory disease vs. reference values in healthy subject [A]. The [Gd-DOTA] was calculated and the Tofts constants were extracted using a non linear fit. [B]

Results: The Tofts constants K^{trans}, K_{ep}, V_e in healthy subjects were detailed for each muscle in Table 1. No statistically significant difference was detected across muscles or between sexes and age groups.

An example of the use of these benchmarks is shown in Figure 1. A patient with a histologicaly proven inflammatory myopathy had abnormal values for K^{trans},= 0.33, K_{ep} = 0.35 and V_e =0.93.

Conclusion: This study provides reference values of Gd-CA enhancement kinetics in thigh muscle. These benchmark curves and extracted Tofts constants, will for the first time make it possible to identify unambiguously and objectively pathological enhancements in various conditions. They will also provide quantitative markers mandatory essential to interpretation of longitudinal studies.

1. Pamboucas C, Schmitz S, Nihoyannopoulos P. Magnetic resonance imaging in the detection of myocardial viability: the role of delayed contrast hyperenhancement. Hellenic journal of cardiology : 2005; 46:108-116.
2. Lutz AM, Weishaupt D, Amann-Vesti BR, et al. Assessment of skeletal muscle perfusion by contrast medium first-pass magnetic resonance imaging: technical feasibility and preliminary experience in healthy volunteers. Journal of magnetic resonance imaging : JMRI 2004; 20:111-121.
3. Tofts PS, Brix G, Buckley DL, et al. Estimating kinetic parameters from dynamic contrast-enhanced t1-weighted MRI of a diffusable tracer: Standardized quantities and symbols. Journal of Magnetic Resonance Imaging 1999; 10:223-232.